Remarks

Claims 1-6, 8, and 10-20 are pending in the subject application. By this Amendment, claims 1, 2, 5, 8, 10, 13, 15, 16, 19, and 20 have been amended. Support for these amendments can be found throughout the subject specification including, for example, at page 2, lines 24-32. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1-6, 8, and 10-20 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Claims 2, 10, and 16 have been rejected under 35 U.S.C. §112, first paragraph. The Office Action states that the limitation "1-30 kD fraction" is unclear and that the disclosure would not support the concept of making or using "1-30 kD fraction." As noted above, the applicant has amended claims 2, 10, and 16 to correct a typographical error and clarify that a "10-30 kD fraction" is obtained. Accordingly, reconsideration and withdrawal of this rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 1-6, 8, and 10-20 have been rejected under 35 U.S.C. §112, second paragraph. In order to expedite prosecution, claims 1, 8, and 15 have been amended to clarify that the claimed material is obtained from ovarian venous blood. The applicant also respectfully submits that the point of rejection related to the protocol has also been addressed by way of amendment. Specifically, claims 5, 13, and 19 have been amended to include active steps for the purifying protocol. In addition, claim 20 has been amended to clarify that sheep are the source of the material. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claims 1, 8, and 15 have been rejected under 35 U.S.C. §102(b) as being anticipated by Hart (*Toxicology*, 61(2):185-194 (1990)). The applicant respectfully traverses this grounds of rejection because the Hart reference does not disclose the unique material, or its use, claimed by the current applicant.

The claimed natural product, obtained from ovarian venous blood is readily distinguishable from the synthetic material disclosed in the cited reference. In addition to their differing sources and chemical characteristics, the claimed material has the remarkable ability to diminish the size and

weight of many organs and tissues throughout the body. As discussed below, the Hart reference does not disclose such a product.

It is a basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra*; *Kalman [v. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

In the current case, the claims specifically recite that the material, obtained from ovarian venous blood, has the ability to reduce organ mass. This material, or a method of using such a material, is not disclosed by Hart. Therefore, an anticipation rejection is improper.

The Hart reference, which was authored by the current applicant, describes a product called clomiphene. The Hart reference does not teach clomiphene to be capable of reducing organ mass. Rather, the Hart reference discloses that clomiphene has the ability to impede hexoestrol-induced growth in organ mass. In the experiments conducted by Hart, clomiphene was administered to rats after hexoestrol treatment. Hexoestrol generally induces weight gain in several principal organs. The Hart reference teaches that pretreatment with clomiphene largely prevented, in a dose-dependent manner, the increase in organ weights induced by hexoestral (p.192 of the Hart reference). Thus, clomiphene appears to be an antagonist of endogenous oestrogen (see p. 193 of the Hart reference).

In contrast, the present invention is directed to a material that causes a reduction in mass in organs such as the pituitary, liver, uterus, ovaries, heart, kidneys, adrenals, and spleen (see figures 1-5 of the application). In addition, as noted above, the claims of the subject invention have been amended to specify the source of the claimed material.

Therefore, the Hart reference fails to teach a material that demonstrates anti-organotrophic effects. The Hart reference also fails to disclose an association between clomiphene and the material

claimed in the subject invention. Thus, the Hart reference does not anticipate the applicant's claimed material, or its use to reduce organ mass. Accordingly, the applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1, 8 and 15 under 35 U.S.C. §102(b) as anticipated by Hart.

Claims 1-3, 8, 10, 11, and 15-17 have been rejected under 35 U.S.C. §102(b) as anticipated by diZerega (U.S. Patent No. 4,734,398). The applicant respectfully traverses this grounds for rejection because the diZerega reference does not disclose a material having the chemical properties or advantageous functional characteristics of the material claimed by the current applicant.

The diZerega reference discloses a follicular regulatory protein (FRP) claimed to inhibit ovarian response to gonadotropins. The diZerega reference only suggests the use of FRP in contraception and, via blockade with an FRP antibody, in the treatment of infertility (col. 3, lines 31-37). The diZerega reference does not describe or suggest the use of FRP in the treatment of ovarian and non-ovarian tissue overgrowth conditions. In fact, no data is disclosed in the diZerega reference relating to general reduction in organ mass. Rather, diZerega only provide bioassay data relating to FRP activity in inhibiting gonadotropin-induced re-growth in preshrunk ovaries. Prevention of re-growth is very different from reducing organ mass

The bioassay described in the diZerega reference involves female rats subjected to hypophysectomy (removal of the pituitary) and oestrogen treatment (see col. 9, line 50 through col. 10, line 45). The gonadotropins LH and FSH were given by injection, with bovine serum albumin or active fractions (col. 9, line 65 through col. 10, line 3). Hypophysectomy causes a marked shrinkage in ovary sizes to below normal levels. This shrinkage was limited by the administration of supplementary estrogen and regrowth in the ovaries was induced by the administration of gonadotropins (col. 10, lines 15-33). When FRP was administered in combination with gonadotropins, gonadotropin-induced ovarian regrowth was interrupted (col. 10, lines 34-52). Thus, the diZerega reference only discloses FRP interruption of ovarian regrowth by inhibiting exogenous gonadotropin effect in the ovary and does not teach the use of FRP in organ mass reduction.

In contrast, the composition of the subject invention reduces organ mass. To assess its anti-organotrophic effect, the claimed material of the subject invention was administered to normal female rats not subject to surgical alteration or other pretreatment. The material of the subject

invention caused a widespread reduction in organ mass. Moreover, the claimed material demonstrated anti-organotrophic effect in organs that are unaffected by gonadotropins, such as the heart and kidneys (see Figures 1-5).

The present invention is directed to a material that exhibits anti-organotrophic effects. The diZerega reference does not disclose or suggest such a material. The Office Action speculates that such claimed effects are either found in diZerega or are so similar to the effects of FRP as to be "inherent" in diZerega. The applicant respectfully submits that no basis or justification for such speculation is available in diZerega.

Under the Patent Laws, a prior art rejection based on inherency is only proper if the prior art necessarily resulted in the claimed subject matter. *In re King*, 801 F2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). Further,

> the doctrine of inherency is available only when the prior inherent event can be established as a certainty. That an event may result from a given set of circumstances is not sufficient to establish anticipation....A prior inherent event cannot be established based on speculation, or where a doubt exists (emphasis added). *Ethyl Molded Product Co. v. Betts Package Inc.*, 9 USPQ2d 1001, 1032-33 (E.D. KY 1988).

As discussed above, it cannot reasonably be stated that the diZerega reference discloses or suggests a material that necessarily reduces organ mass. From a reading of diZerega, one skilled in the art would only expect FRP to impede gonadotropin-induced regrowth in ovaries. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102 is respectfully requested.

Claims 1-5, 8, 10-13, and 15-19 have been rejected under 35 U.S.C. §102(b) as anticipated by diZerega or, in the alternative, under 35 U.S.C. §103(a) as obvious over diZerega. Also, claims 1-6, 8, and 10-20 have been rejected under 35 U.S.C. §103(a) as obvious over diZerega. The applicant respectfully traverses these grounds of rejection because the cited reference does not teach or suggest the claimed material or its use to reduce organ mass.

The shortcomings of the diZerega reference have been discussed above. diZerega only discloses the ability of FRP to impede gonadotropin-induced regrowth in preshrunk ovaries, which does not constitute organ mass reduction. Moreover, there is no teaching or suggestion by diZerega

that the use of FRP would reduce organ mass. The applicant's claims explicitly recite the material's ability to reduce organ mass as a claim limitation.

As noted above, for an anticipation rejection to be proper, a single prior art reference must disclose, within its four corners, each and every element of the claimed invention. In *Dewey & Almy Chem. Co. v. Mimex Co.*, Judge Learned Hand wrote:

> No doctrine of the patent law is better established than that a prior patent . . . to be an anticipation must bear within its four corners adequate directions for the practice [of the subsequent invention] . . . if the earlier disclosure offers no more than a starting point . . . if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation. 124 F.2d 986, 990; 52 USPQ 138 (2nd Cir. 1942).

Because the diZerega reference does not teach or suggest materials and methods for reducing organ mass the applicant's claims are not anticipated by the diZerega reference. Thus, the applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. §102 based on diZerega.

With regard to the issue of obviousness, nothing in the diZerega reference would have led the skilled artisan to the advantageous materials and methods claimed by the current applicant. As noted above, no physical or function similarities exist between the current applicant's material and the composition described in the diZerega reference.

A finding of obviousness is proper only when the prior art contains a suggestion or teaching of the claimed invention. Here, it is only the applicant's disclosure that provides such a teaching, and the applicant's disclosure cannot be used to reconstruct the prior art for a rejection under 35 USC §103. This was specifically recognized by the CCPA in *In re Sponnoble*, 56 CCPA 823, 160 USPQ 237, 243 (1969):

> The Court must be ever alert not to read obviousness into an invention on the basis of the applicant's own statements; that is we must review the prior art without reading into that art appellant's teachings. *In re Murray*, 46 CCPA 905, 268 F.2d 226, 112 USPQ 364 (1959); *In re Sprock*, 49 CCPA 1039, 301 F.2d 686, 133 USPQ 360 (1962). The issue, then, is whether the teachings of the prior art would, in and of themselves and without the benefits of appellant's disclosure, make the invention as a whole, obvious. *In re Leonor*, 55 CCPA 1198, 395 F.2d 801, 158 USPQ 20 (1968). (Emphasis in original)

The mere fact that the purported prior art could have been modified or applied in a manner to yield the applicant's invention would not have made the modification or application obvious unless the prior art suggested the desirability of the modification. *In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Moreover, as expressed by the CAFC, to support a §103 rejection, "[b]oth the suggestion and the expectation of success must be founded in the prior art . . . ." *In re Dow Chemical Co., supra* at 1531. In the diZerega reference, one finds neither.

The diZerega reference does not disclose or suggest a material that can reduce organ mass. Rather, diZerega only provides FRP, a material that impedes gonadotropin-induced regrowth in preshrunk ovaries. Thus, the diZerega reference does not describe, teach, nor suggest a material having the advantageous characteristics of the claimed invention. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on diZerega is respectfully requested.

In view of the foregoing remarks and the amendments above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicant also invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

David Saliwanchik

David R. Saliwanchik
Patent Attorney
Registration No. 46,853
Phone: 352-375-8100
Fax No.: 352-372-5800
Address: 2421 N.W. 41st Street, Suite A-1
Gainesville, FL 32606-6669

DRS/la
Attachment: Marked-Up Version of Amended Claims
Petition and Fee for Extension of Time

Marked-up Version of Substituted Claims

Claim 1 (amended):

A material having the ability to reduce organ mass, the material being obtain[abl]ed by:

collecting ovarian venous blood from a female mammal;

preparing ovarian venous plasma from the blood; and

at least partially purifying said material from the plasma.

Claim 2 (amended):

The material according to claim 1, wherein the purifying comprises obtaining the 10-30 kD fraction.

Claim 5 (amended):

The material according to claim 1, wherein the purifying comprises the following protocol:

clearing plasma [cleared] by centrifugation;

spinning the cleared plasma [spun] to give a nominal 0-30 kD fraction;

spinning the nominal 0-30 kD fraction [spun] to give a nominal 10-30 kD sub-fraction;

concentrating and gel-filtering the nominal 10-30 kD sub-fraction [concentrated and gel-filtered] to give a nominal 10-20 kD sub-fraction;

concentrating and buffer-diluting the nominal 10-20 kD sub-fraction repeatedly [concentrated and buffer-diluted,];

applying the concentrate and buffer-diluted nominal 10-20 kD sub-fraction repeatedly [applied] to an ion exchange column eluted with a gradient of 0-.3 M NaCl; and

[eluate]divid[ed]ing the eluate into 0-0.1 M, 0.1-0.2 M and 0.2-0.3 M NaCl ion exchange fractions.

Claim 8 (amended):

A pharmaceutical composition comprising a material having the ability to reduce organ mass, the material being obtain[abl]ed by:

collecting ovarian venous blood from a female mammal;

preparing ovarian venous plasma from the blood; and

at least partially purifying said material from the plasma

and a pharmaceutically acceptable excipient or carrier.

Claim 10 (amended):

The pharmaceutical composition, according to claim 8, wherein the purifying comprises obtaining the 10-30 kD fraction.

Claim 13 (amended):

The pharmaceutical composition, according to claim 8, wherein the purifying comprises the following protocol:

clearing plasma [cleared]by centrifugation;

spinning the cleared plasma [spun]to give a nominal 0-30 kD fraction;

spinning the nominal 0-30 kD fraction [spun]to give a nominal 10-30 kD sub-fraction;

concentrating and gel-filtering the nominal 10-30 kD sub-fraction [concentrated and gel-filtered]to give a nominal 10-20 kD sub-fraction;

concentrating and buffer-diluting nominal 10-20 kD sub-fraction repeatedly[concentrated and buffer-diluted,];

applying the concentrated and buffer-diluted nomical 10-20 kD sub-fraction repeatedly [applied]to an ion exchange column eluted with a gradient of 0-.3 M NaCl; and

[eluate]divid[ed]ing the eluate into 0-0.1 M, 0.1-0.2 M and 0.2-0.3 M NaCl ion exchange fractions.

Claim 15 (amended):

A method for treating organ or tissue hypertrophy wherein said method comprises administering, to a patient in need of such treatment, an effective amount of a material having the ability to reduce organ mass, the material being obtain[abl]ed by:

collecting ovarian venous blood from a female mammal;

preparing ovarian venous plasma from the blood; and

at least partially purifying said material from the plasma.

Claim 16 (amended):

The method, according to claim 15, wherein the purifying comprises obtaining the 10-30 kD fraction.

Claim 19 (amended):

The method, according to claim 15, wherein the purifying comprises the following protocol:

clearing plasma [cleared]by centrifugation;

spinning the cleared plasma [spun]to give a nominal 0-30 kD fraction;

spinning the nominal 0-30 kD fraction [spun]to give a nominal 10-30 kD sub-fraction;

concentrating and gel-filtering the nominal 10-30 kD sub-fraction [concentrated and gel-filtered]to give a nominal 10-20 kD sub-fraction;

concentrating and buffer-diluting the nominal 10-20 kD sub-fraction repeatedly[concentrated and buffer-diluted,];

applying the concentrated and buffer-diluted nominal 10-20 kD subfraction repeatedly [applied]to an ion exchange column eluted with a gradient of 0-.3 M NaCl; and

[eluate]divid[ed]ing the eluate into 0-0.1 M, 0.1-0.2 M and 0.2-0.3 M NaCl ion exchange fractions.

Claim 20 (amended):

The method, according to claim 15, wherein the mammal from which the ovarian venous blood is collected is a sheep.